



Differentiating Persistently Positive COVID-19 Cases from SARS-CoV-2 Reinfections Utilizing Laboratory Evidence, Virginia, 2020 – 2021



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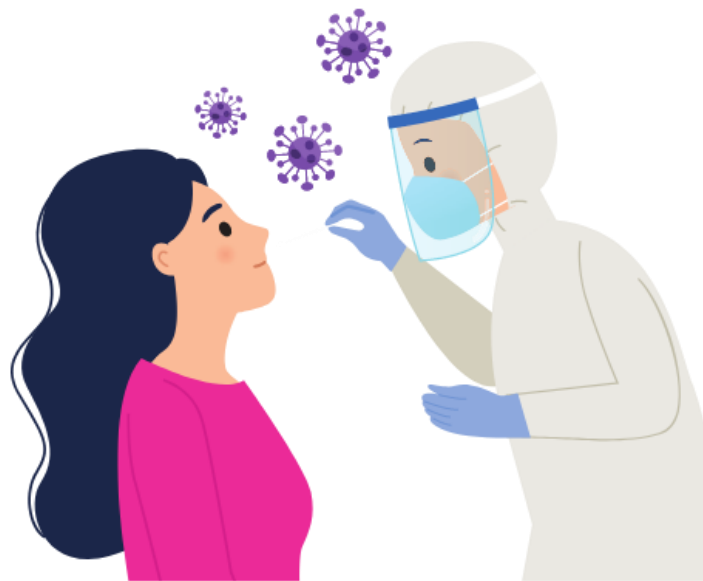


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Objectives

- After the session, the attendee will be able to highlight the value of conducting a real-time epidemiologic research study during an ongoing pandemic supported by genomic laboratory evidence.
- Participants will be able to understand the importance of whole genome sequencing (WGS) as a method for differentiating persistently positive COVID-19 cases from SARS-CoV-2 reinfection.
- Attendees will be able to compare the advantages and disadvantages of using genomic sequencing paired with case-level epidemiologic interview data to monitor genetic changes in the virus, over time, through enhanced surveillance of SARS-CoV-2 variants.

Background



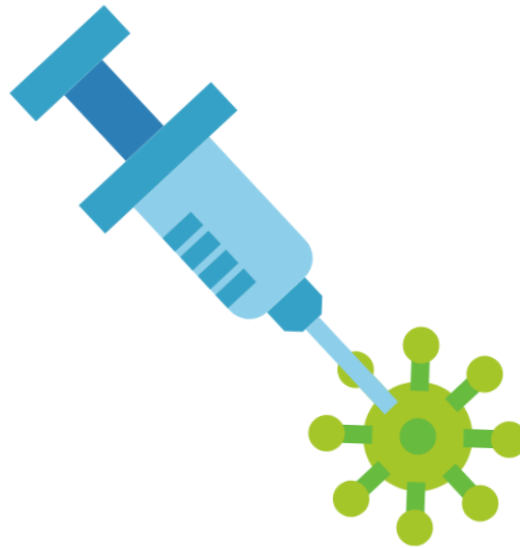
2020 Research Questions - Re-interviews

- I. How do persistently positive COVID-19 cases' initial infection differ from subsequent SARS-CoV-2 reinfections, considering indicators of disease severity (symptoms, pneumonia, hospitalization, death)?
- II. Is reinfection risk greater in congregate settings or for patients with repeat exposures to confirmed cases?
- III. What can be learned by comparing reinfection cases to others with the same exposures in a healthcare facility outbreak?






*Re-interviews: to improve exposure and disease severity data quality

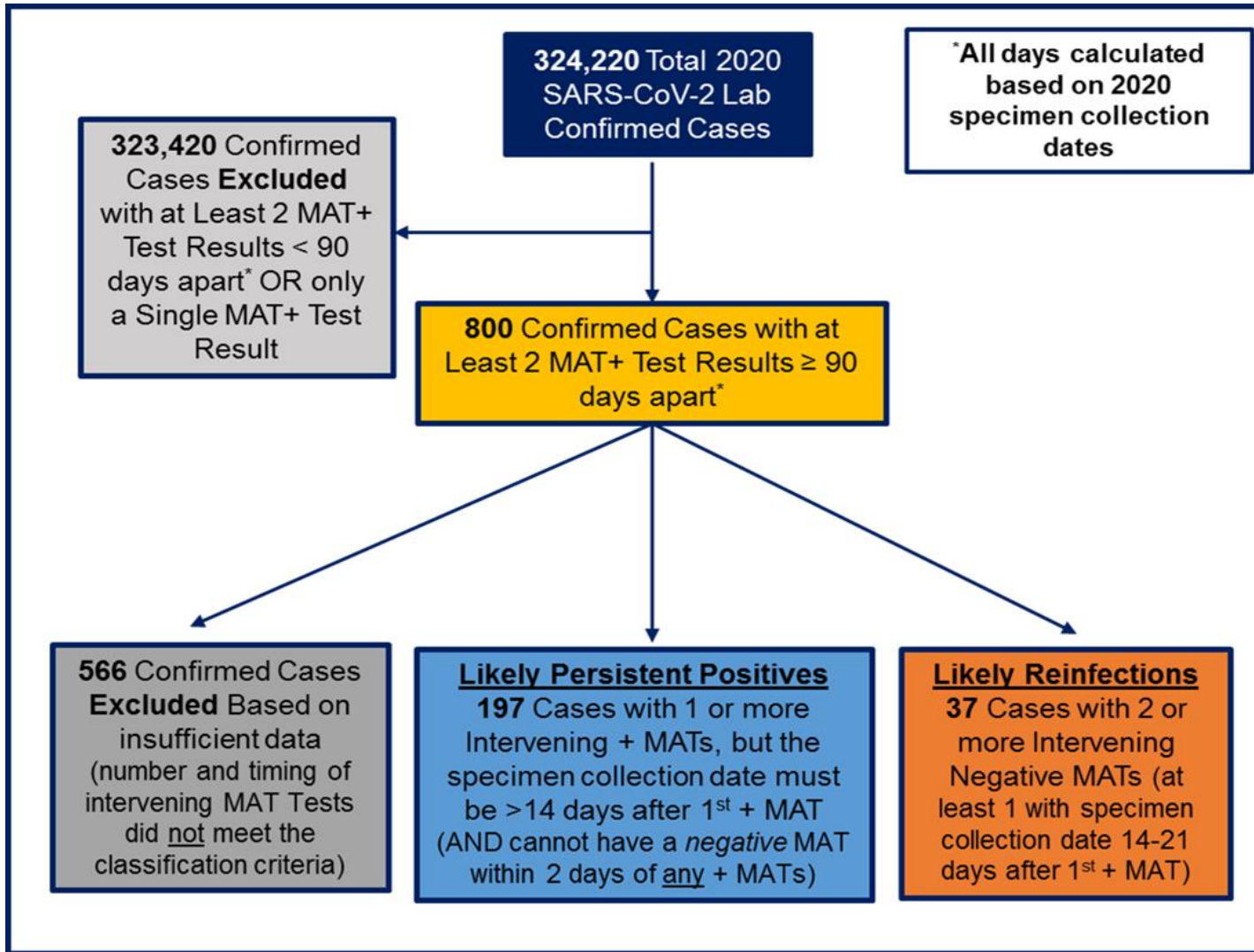
Methods



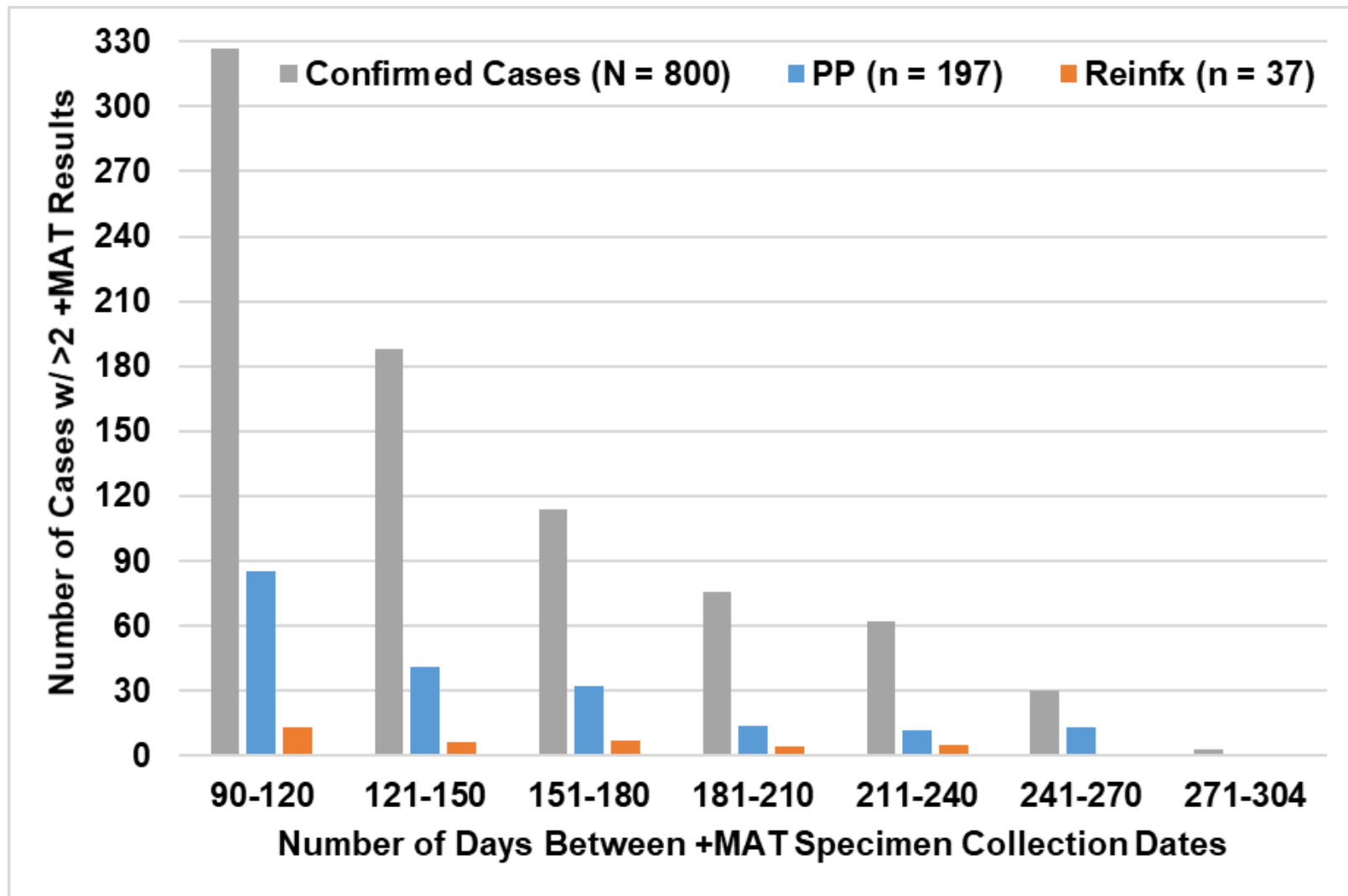
Expanded 2020 Study - Case Definitions

- 2020 COVID-19 cases with 2 +MATs >90 days apart (N=800) using these revised criteria
- **Likely Persistent Positive (PP) cases:** those with 1 or more intervening +MAT during the 90 day interval, but the specimen collection date must be >14 days after 1st +MAT (and without a neg MAT w/in 2 days of +) 
- **Likely Reinfections (Reinfx):** those with   2 or more intervening neg MATs (at least 1 with specimen collection date 14-21 days after initial +)
- Cases with insufficient evidence or data to classify as either Persistent Positive cases or Reinfections

Study Selection Criteria for Likely Persistent Positive COVID-19 Cases and SARS-CoV-2 Reinfections, 2020 Analysis



Days Between Confirmatory Test Results for 2020 COVID-19 Cases, with Two or More Positive MAT Specimens Collected >90 days Apart



2021 Revised CSTE Case Definition



Person previously enumerated as a “Confirmed” (non-genomic sequencing) or “Probable” case

Yes

SARS-CoV-2 RNA ‘detected’ or SARS-CoV-2 specific Ag ‘detected’ by CLIA-certified provider or laboratory AND specimen collection date >90 days later?

Yes

Re-infection Case

Person previously enumerated as a “Confirmed” case based on genomic sequencing

Yes

SARS-CoV-2 sequencing results from a new positive specimen demonstrates a different lineage?

Yes

Re-infection Case

Results



2020 – 2021 Results

2021: Total possible SARS-CoV-2 reinfections

(2 MAT+s >90 days apart, includes 2021 only Sp. Coll. Dt.)

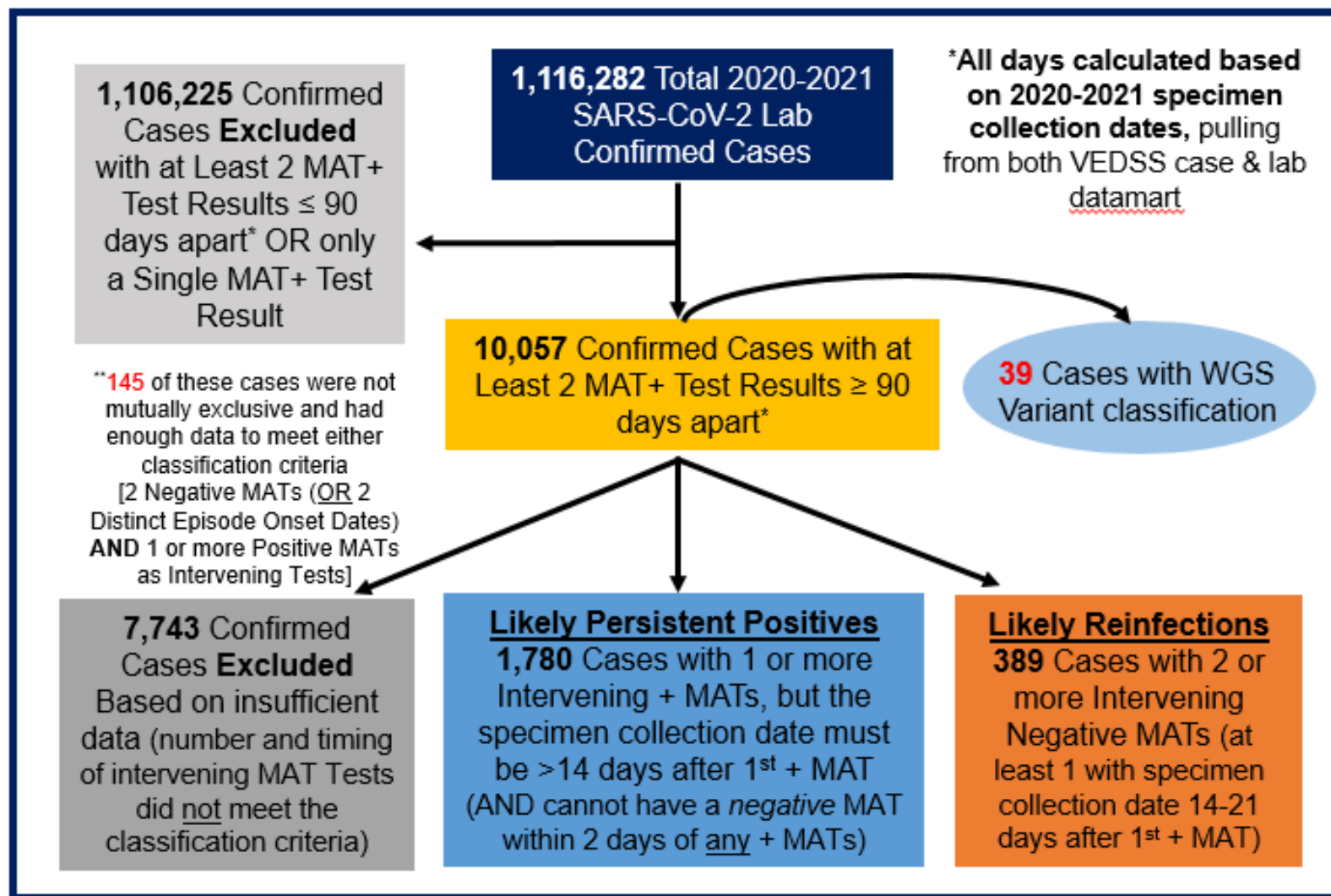
- N=1,466 w/ Case Count=1 (Confirmed only)
- n=265 Likely Persistent Positive COVID-19 cases
- n=75 Likely Reinfections

'20-'21: Total possible SARS-CoV-2 reinfections

(2 MAT+s >90 days apart, includes '20-'21 Sp. Coll. Dt.)

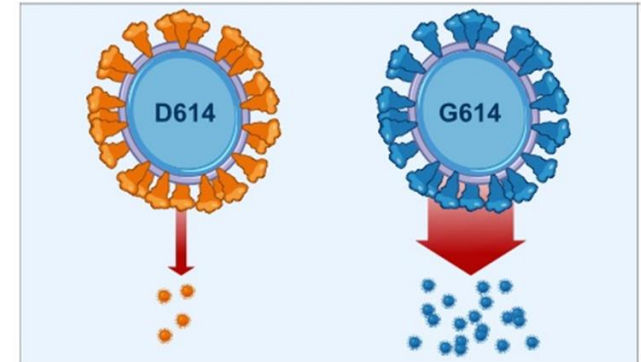
- N=10,057 w/ Case Count=1 (Confirmed only)
- n=1,780 Likely Persistent Positive COVID-19 cases
- n=389 Likely Reinfections

Study Selection Criteria for Likely Persistent Positive COVID-19 Cases and SARS-CoV-2 Reinfections '20-'21 Analysis

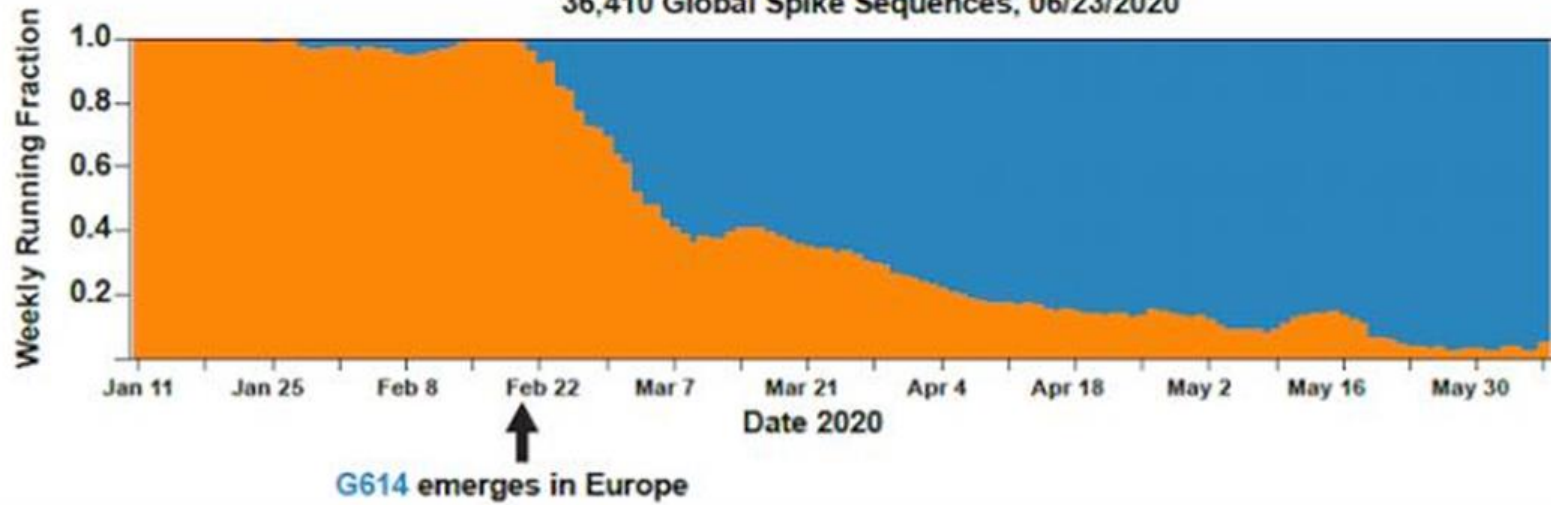


Early 2020: 'DOUG' mutation & Variants of Unknown Significance

Magnitude of Infection



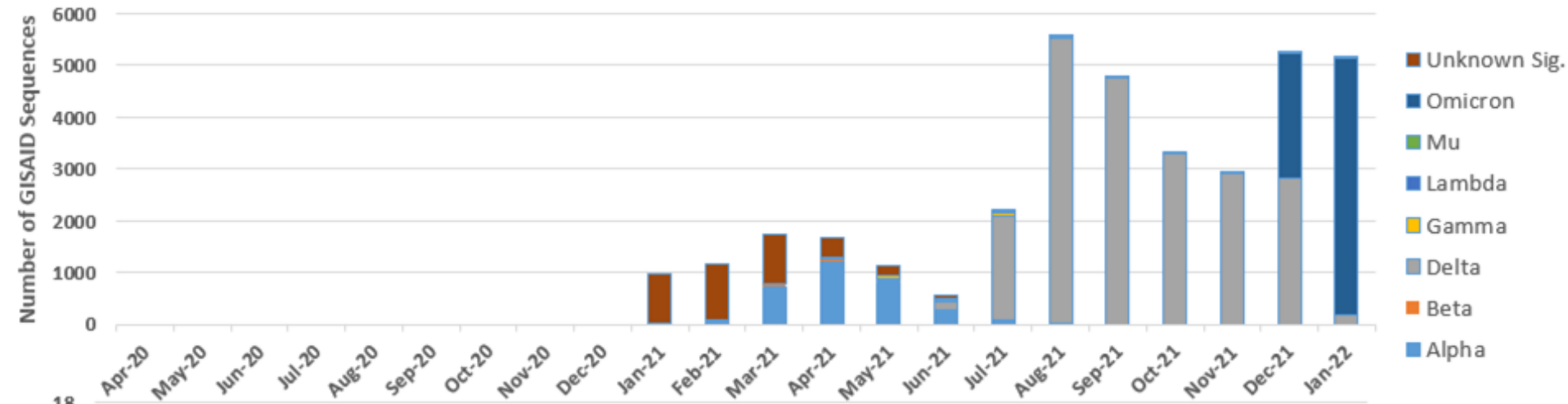
Global Transition from D614 to G614 variants
36,410 Global Spike Sequences, 06/23/2020



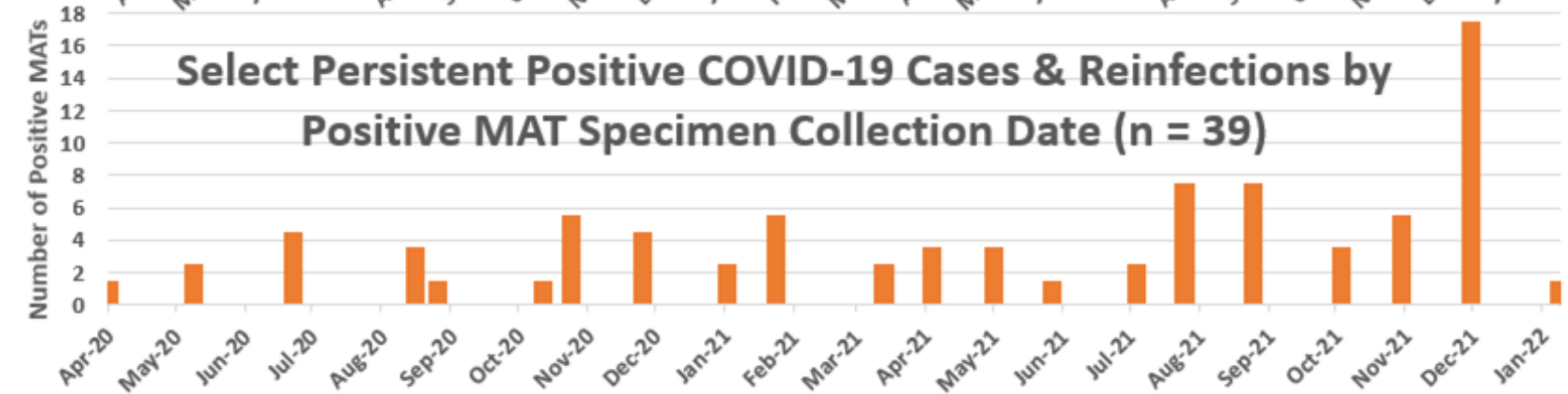
<https://img-labmanager.s3.amazonaws.com/assets/articleNo/23187/img/42980/july3-2020-lanl-2-covid-19-strain-graph.jpg>

https://www.sheffield.ac.uk/news/polopoly_fs/1.8922821/image/covidvirus.jpg

SARS-CoV-2 Variant Lineages by Specimen Collection Date

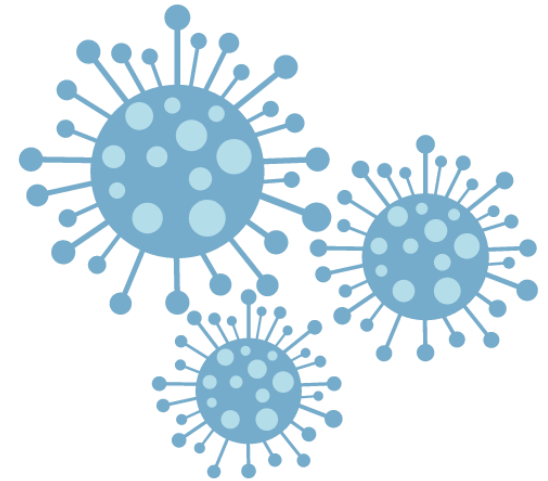


Select Persistent Positive COVID-19 Cases & Reinfections by Positive MAT Specimen Collection Date (n = 39)



Discussion

Case Studies



Reinfection Case Studies Timeline

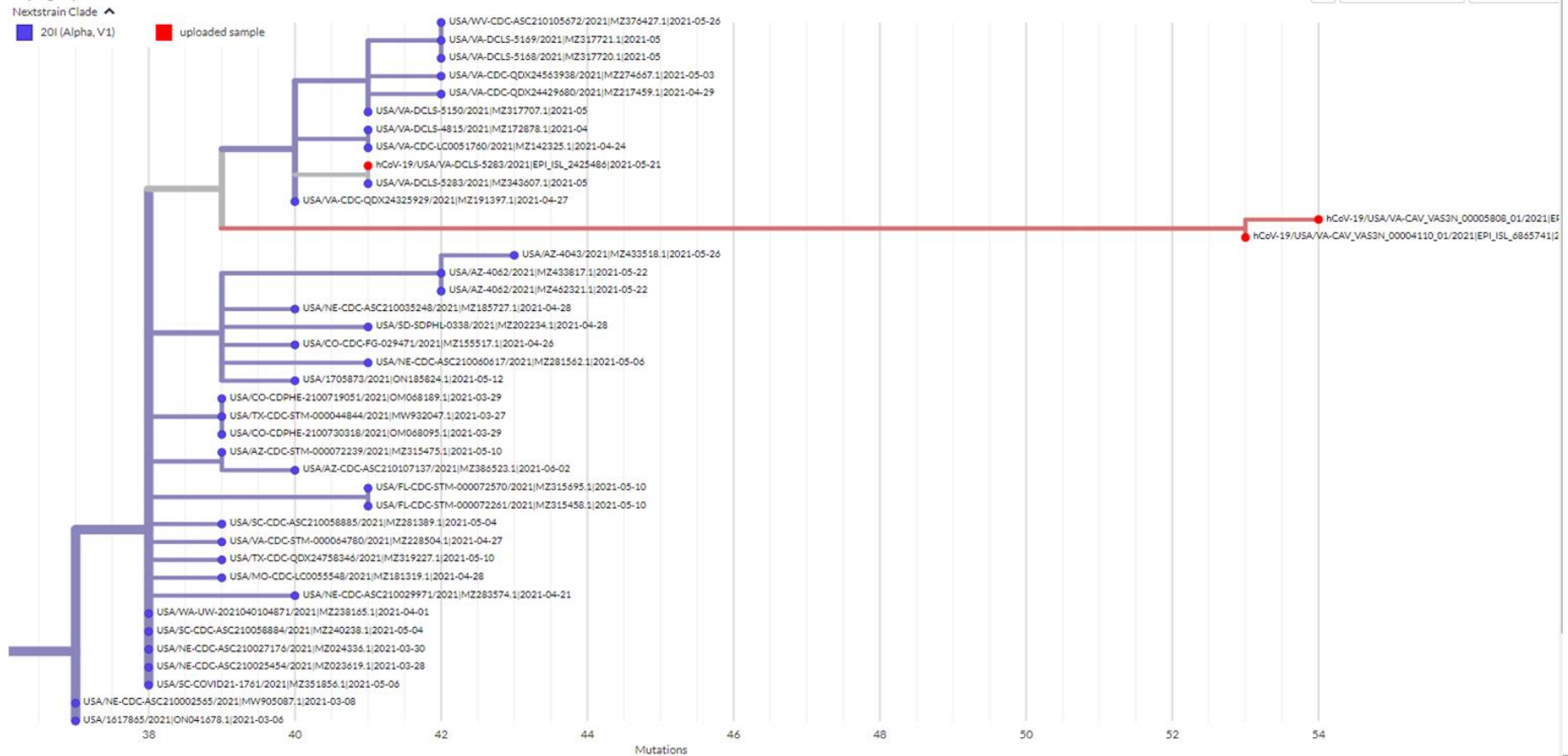
Timeline of events for each patient (PCR+ sp. coll. date used as proxy if onset date is unknown)



True Persistent Positive Case

ID	Sequence name	QC	Clade	Pango lineage (Nextclade)	Mut.	non-ACGTN	Ns	Gaps	Ins.	FS	SC	Nucleotide sequence
0	hCoV-19/USA/VA-DCLS-5283/2021/EPI_ISL_2425486	NMTCFS	20I (Alpha, V1)	B.1.1.7	41	0	12	19	0	0	0 (1)	
1	hCoV-19/USA/VA-CAV_VAS3N_00004110_01/2021/EPI_ISL_68657412	NMTCFS	20I (Alpha, V1)	B.1.1.7	51	0	295	19	0	0	0 (1)	
2	hCoV-19/USA/VA-CAV_VAS3N_00005808_01/2021/EPI_ISL_68657412	NMTCFS	20I (Alpha, V1)	B.1.1.7	52	0	1201	19	0	0	0 (1)	

Phylogeny

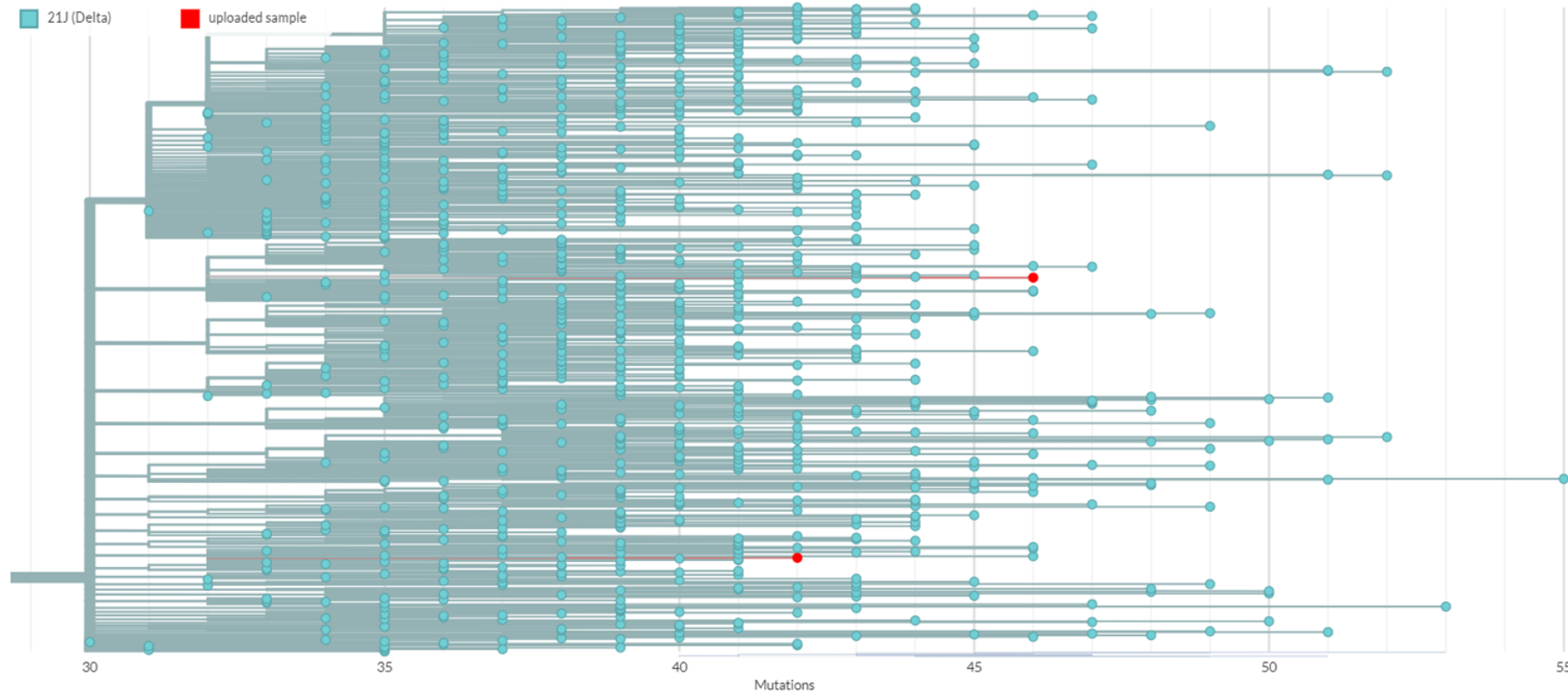


True Reinfection

ID	Sequence name	QC	Clade	Pango lineage (Nextclade)	Mut.	non-ACGTN	Ns	Gaps	Ins.	FS	SC	Nucleotide sequence
0	hCoV-19/USA/VA-CAV_VAS3N_00005585_01/20	NMPCFS	21J (Delta)	AY.39	41	0	373	47	0	0	0	
1	hCoV-19/USA/VA-CAV_VAS3N_00005675_01/20	NMPCFS	21J (Delta)	AY.103	46	0	833	13	0	0	0	

Phylogeny
Nextstrain Clade ^

21J (Delta) uploaded sample



Acknowledgements

